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PATENT COOPERATION *** ATY

	From the INTERNATIONAL BUREAU
PCT	То:
NOTIFICATION OF ELECTION (PCT Rule 61.2)	Commissioner US Department of Commerce United States Patent and Trademark Office, PCT 2011 South Clark Place Room CP2/5C24 Arlington, VA 22202 ETATS-UNIS D'AMERIQUE
Date of mailing: 01 March 2001 (01.03.01)	in its capacity as elected Office
International application No.: PCT/JP00/05523	Applicant's or agent's file reference: 2628WO0P
International filing date: 18 August 2000 (18.08.00)	Priority date: 20 August 1999 (20.08.99)
Applicant: OHKAWA, Shigenori et al	
1. The designated Office is hereby notified of its election made X in the demand filed with the International preliminary 29 September	Examining Authority on: 2000 (29.09.00) ational Bureau on:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland

Authorized officer:

J. Zahra

Telephone No.: (41-22) 338.83.38

Facsimile No.: (41-22) 740.14.35





Eur päisches Pat ntamt

Zweigstelle in Den Haag Recherchenabteilung European Patent Office

Branch at The Hague Search division Office uropeen des brevets

Departement à La Haye Division de la recherche

Lewin, John Harvey Takeda Patent Office, 11-12 Charles II Street London SW1Y 4QU GRANDE BRETAGNE



Datum/Date 06.02.03

Zeichen/Ref./Ref.

2628EPOW

Anmeldung Nr./Application No./Demande nº./Patent Nr./Patent No./Brevet nº.

00953479.3-2117-JP0005523

Anmelder/Applicant/Demandeur/Patentinhaber/Proprietor/Titulaire
Takeda Chemical Industries, Ltd.

COMMUNICATION

The European Patent Office herewith transmits as an enclosure the European search report for the above-mentioned European patent application.

If applicable, copies of the documents cited in the European search report are attached.

Additional set(s) of copies of the documents cited in the European search report is (are) enclosed as well.

REFUND OF THE SEARCH FEE

If applicable under Article 10 Rules relating to fees, a separate communication from the Receiving Section on the refund of the search fee will be sent later.





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2

SUPPLEMENTARY PARTIAL EUROPEAN SEARCH REPORT

Application Number

which under Rule 45 of the European Patent ConventionEP 00 95 3479 shall be considered, for the purposes of subsequent proceedings, as the European search report

1	DOCUMENTS CONSIDE	RED TO BE RELEVANT				
Category	Citation of document with in of relevant pass	dication, where appropriate,	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.CI.7)		
P,X	EP 0 992 496 A (PFI) 12 April 2000 (2000- compounds of formula group C(a) (see page	-04-12) a (I), in particular	1	A61K31/407 A61K31/55 A61P9/10 A61P25/28 A61P25/16		
Y	US 5 478 844 A (AON 26 December 1995 (19 * column 1, line 330 claims 1,9; table 1	995-12-26) 5 - column 2, line 11;	1-32	A61P13/02 A61P9/08 C07D491/04 A61K31/425 A61K31/40		
Y	LTD) 13 December 198	EDA CHEMICAL INDUSTRIES B9 (1989-12-13) cage 2, line 22; claim	1-32	A01K31/40		
A	US 5 420 289 A (MUS 30 May 1995 (1995-0 * column 3, line 55		1-32			
				TECHNICAL FIELDS SEARCHED (Int.CI.7)		
				C07D		
				A61K		
The su	applementary search report has be a available at the start of the sear	een based on the last set of claims valid ch.	3			
INCO	MPLETE SEARCH					
not compl be carried	The Search Division considers that the present application, or some or all of its claims, does/do not comply with the EPC to such an extent that a meaningful search into the state of the art cannot be carried out, or can only be carried out partially, for the following claims: Claims searched completely:					
Claims se	earched incompletely :					
Claims not searched: Reason for the limitation of the search:						
					tre: EPC	atment of the human/), the search has be
	Prace of search	Date of completion of the search		Examiner		
	MUNICH	24 January 2003	Wön	rth, C		
CATEGORY OF CITED DOCUMENTS T: theory or principle underlying the invention E: earlier patent document, but published on, or A: particularly relevant if combined with another document of the same category A: technological background T: theory or principle underlying the invention E: earlier patent document, but published on, or after the filing date D: document cited in the application L: document of the reasons						

ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO.

EP 00 95 3479

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

24-01-2003

	Patent documer cited in search rep		Publication date		Patent family member(s)	Publication date
EP	0992496	A	12-04-2000	BR EP JP US US	9904162 A 0992496 A1 2000095764 A 6147089 A 6310075 B1	12-09-2000 12-04-2000 04-04-2000 14-11-2000 30-10-2001
US	5478844	A	26-12-1995	USS ARA CDE LES HUUEL LE L	5594154 A 5770772 A 127797 T 1100381 A3 2054619 A1 69112989 D1 483772 T3 0483772 A1 2077138 T3 3017981 T3 60258 A2 9500528 A3 913724 A1 70668 B1 2672423 B2 5140142 A 202463 B1 5376681 A 1071165 A 921890 A 921572 A 973061 A 2087473 C1	14-01-1997 23-06-1998 15-09-1995 18-04-2000 02-05-1992 19-10-1995 22-01-1996 06-05-1992 16-11-1995 29-02-1996 28-08-1992 30-10-1995 22-05-1992 11-12-1996 05-11-1997 08-06-1993 15-06-1999 27-12-1994 21-04-1993 04-03-1998 26-03-1993 26-03-1993 26-03-1993
EP	0345593	A	13-12-1989	AT CA DE DE EP JP US	93231 T 1339505 A1 68908481 D1 68908481 T2 0345593 A1 2076869 A 2855340 B2 4978761 A	15-09-1993 21-10-1997 23-09-1993 09-12-1993 13-12-1989 16-03-1990 10-02-1999 18-12-1990
US	5420289	A	30-05-1995	US AU MX WO AU AU	5229516 A 4669493 A 9304138 A1 9401407 A2 643996 B2 7740491 A	20-07-1993 31-01-1994 29-04-1994 20-01-1994 02-12-1993 31-05-1991

ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO.

O

EP 00 95 3479

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

24-01-2003

Patent docum cited in search r		Publication date	Patent family member(s)	Publication date
US 5420289	A	BR CA EP FI HU IE JP PT WO CA	0502106 A1 921865 A 63407 A2 903872 A1 5502222 T 95692 A 9106537 A2	15-09-1992 28-04-1991 09-09-1992 24-04-1992 30-08-1993 22-05-1991 22-04-1993 13-09-1991 16-05-1991 28-04-1991
				·

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION CONCERNING SUBMISSION OR TRANSMITTAL OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

Date of mailing (day/month/your)

TAKAHASHI, Shuichi Osaka Plant of Takeda Chemical Industries, Ltd.

17-85, Jusohonmachi 2-chome

Yodogawa-ku . Osaka-shi Osaka 532-0024

JAPON

06 November 2000 (06.11.00)	(ALL 3)长1/至 (B)
Applicant's or agent's file reference 2628WO0P	IMPORTANT NOTIFICATION
International application No. PCT/JP00/05523	International filing date (day/month/year) 18 August 2000 (18.08.00)
International publication date (day/month/year) Not yet published	Priority date (day/month/year) 20 August 1999 (20.08.99)
Applicant	

TAKEDA CHEMICAL INDUSTRIES, LTD. et al

- The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
- This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.
- An asterisk(*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
- The letters "NR" appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

Country or regional Office Date of receipt Priority application No. Priority date of priority document or PCT receiving Office JP 05 Octo 2000 (05.10.00) 20 Augu 1999 (20.08.99) 11/234718

> The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland

Authorized officer

Khemais BRAHMI

003639018

Facsimile No. (41-22) 740.14.35

Telephone No. (41-22) 338.83.38

Form PCT/IB/304 (July 1998)

16

PATENT COOPERATION TREATY

型番番 G·M Fo V お 長 PCT

To:

NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

From the INTERNATIONAL BUREAU
To:

TAKAHASHI, Shuichi Osaka Plant of Takeda Chemical Industries, Ltd.

17-85, Jusohonmachi 2-chome

Yodogawa-ku Osaka-shi

Osaka 532-0024 JAPON



Date of mailing (day/month/year)

01 March 2001 (01.03.01)

Applicant's or agent's file reference 2628WOOP

International application No. PCT/JP00/05523

International filing date (day/month/year)
18 August 2000 (18.08.00)

Priority date (day/month/year)
20 August 1999 (20.08.99)

IMPORTANT NOTICE

Applicant

TAKEDA CHEMICAL INDUSTRIES, LTD. et al

 Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice: AU,KR,US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:

AE,AG,AL,AM,AP,AZ,BA,BB,BG,BR,BY,BZ,CA,CN,CR,CU,CZ,DM,DZ,EA,EE,EP,GD,GE,HR,HU,ID,IL,IN,IS,JP,KG,KZ,LC,LK,LR,LT,LV,MA,MD,MG,MK,MN,MX,MZ,NO,NZ,OA,PL,RO,RU,SG,SI,SK,

TJ,TM,TR,TT,UA,UZ,VN,YU,ZA
The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

 Enclosed with this Notice is a copy of the international application as published by the International Bureau on 01 March 2001 (01.03.01) under No. WO 01/14384

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a demand for international preliminary examination must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the national phase, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Authorized officer

J. Zahra

Facsimile No. (41-22) 740.14.35

Telephone No. (41-22) 338.83.38



PATENT COOPERATION TREATY

PCT

INFORMATION CONCERNING ELECTED OFFICES NOTIFIED OF THEIR ELECTION

(PCT Rule 61.3)

From the INTERNATIONAL BUREAU

To:

JAPON

TAKAHASHI, Shuichi Osaka Plant of Takeda Chemical Industries, Ltd. 17-85, Jusohonmachi 2-chome Yodogawa-ku Osaka-shi Osaka 532-0024

Date of mailing (day/month/year) 01 March 2001 (01.03.01)

Applicant's or agent's file reference 2628WO0P

IMPORTANT INFORMATION

International application No. PCT/JP00/05523

International filing date (day/month/year)
18 August 2000 (18.08.00)

Priority date (day/month/year) 20 August 1999 (20.08.99)

Applicant

TAKEDA CHEMICAL INDUSTRIES, LTD. et al

1. The applicant is hereby informed that the International Bureau has, according to Article 31(7), notified each of the following Offices of its election:

AP:GH,GM,KE,LS,MW,MZ,SD,SL,SZ,TZ,UG,ZW
EP:AT,BE,CH,CY,DE,DK,ES,FI,FR,GB,GR,IE,IT,LU,MC,NL,PT,SE

National :AU,BG,CA,CN,CZ,IL,JP,KR,MN,NO,NZ,PL,RO,RU,SK,US

The following Offices have waived the requirement for the notification of their election; the notification will be sent to them by the International Bureau only upon their request:

EA: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

OA:BF,BJ,CF,CG,CI,CM,GA,GN,GW,ML,MR,NE,SN,TD,TG

National :AE,AG,AL,AM,AZ,BA,BB,BR,BY,BZ,CR,CU,DM,DZ,EE,GD,GE,HR,HU,ID,IN,IS,KG,KZ,LC,LK,LR,LT,LV,MA,MD,MG,MK,MX,MZ,SG,SI,TJ,TM,TR,TT,UA,UZ,VN,YU,

ZΑ

3. The applicant is reminded that he must enter the "national phase" before the expiration of 30 months from the priority date before each of the Offices listed above. This must be done by paying the national fee(s) and furnishing, if prescribed, a translation of the international application (Article 39(1)(a)), as well as, where applicable, by furnishing a translation of any annexes of the international preliminary examination report (Article 36(3)(b) and Rule 74.1).

Some offices have fixed time limits expiring later than the above-mentioned time limit. For detailed information about the applicable time limits and the acts to be performed upon entry into the national phase before a particular Office, see Volume II of the PCT Applicant's Guide.

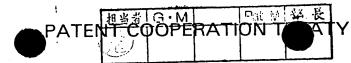
The entry into the European regional phase is postponed until 31 months from the priority date for all States designated for the purposes of obtaining a European patent.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Authorized officer:

J. Zahra

Facsimile No. (41-22) 740.14.35

Telephone No. (41-22) 338.83.38





NOTIFICATION OF RECEIPT OF **RECORD COPY**

(PCT Rule 24.2(a))

From the INTERNATIONAL BUREAU

To:

TAKAHASHI, Shuichi Osaka Plant of Takeda Chemical Industries, Ltd.

17-85, Jusohonmachi 2-chome

Yodogawa-ku Osaka-shi Osaka 532-0024

JAPON

Date of mailing (day/month/year) IMPORTANT NOTIFICATION 13 September 2000 (13.09.00) International application No. Applicant's or agent's file reference PCT/JP00/05523 2628WO0P

The applicant is hereby notified that the International Bureau has received the record copy of the international application as detailed below.

Name(s) of the applicant(s) and State(s) for which they are applicants:

TAKEDA CHEMICAL INDUSTRIES, LTD. (for all designated States except US) OHKAWA, Shigenori et al (for US)

International filing date Priority date(s) claimed

18 August 2000 (18.08.00) 20 August 1999 (20.08.99)

Date of receipt of the record copy by the International Bureau

04 September 2000 (04.09.00)

List of designated Offices

AP:GH,GM,KE,LS,MW,MZ,SD,SL,SZ,TZ,UG,ZW

EA:AM,AZ,BY,KG,KZ,MD,RU,TJ,TM

EP:AT,BE,CH,CY,DE,DK,ES,FI,FR,GB,GR,IE,IT,LU,MC,NL,PT,SE

OA:BF,BJ,CF,CG,CI,CM,GA,GN,GW,ML,MR,NE,SN,TD,TG

National :AE,AG,AL,AM,AU,AZ,BA,BB,BG,BR,BY,BZ,CA,CN,CR,CU,CZ,DM,DZ,EE,GD,GE,HR,HU, ID,IL,IN,IS,JP,KG,KR,KZ,LC,LK,LR,LT,LV,MA,MD,MG,MK,MN,MX,MZ,NO,NZ,PL,RO,RU,SG,SI,

SK,TJ,TM,TR,TT,UA,US,UZ,VN,YU,ZA

ATTENTION

The applicant should carefully check the data appearing in this Notification. In case of any discrepancy between these data and the indications in the international application, the applicant should immediately inform the International Bureau.

In addition, the applicant's attention is drawn to the information contained in the Annex, relating to:

time limits for entry into the national phase

confirmation of precautionary designations

requirements regarding priority documents

A copy of this Notification is being sent to the receiving Office and to the International Searching Authority.

The International Bureau f WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland

Authorized officer:

Shinji IGARASHI

Telephone No. (41-22) 338.83.38

Facsimile No. (41-22) 740.14.35

003519954



INFORMATION ON TIME LIMITS FOR ENTERING THE NATIONAL PHASE

The applicant is reminded that the "national phase" must be entered before each of the designated Offices indicated in the Notification of Receipt of Record Copy (Form PCT/IB/301) by paying national fees and furnishing translations, as prescribed by the applicable national laws.

The time limit for performing these procedural acts is 20 MONTHS from the priority date or, for those designated States which the applicant elects in a demand for international preliminary examination or in a later election, 30 MONTHS from the priority date, provided that the election is made before the expiration of 19 months from the priority date. Some designated (or elected) Offices have fixed time limits which expire even later than 20 or 30 months from the priority date. In other Offices an extension of time or grace period, in some cases upon payment of an additional fee, is available.

In addition to these procedural acts, the applicant may also have to comply with other special requirements applicable in certain Offices. It is the applicant's responsibility to ensure that the necessary steps to enter the national phase are taken in a timely fashion. Most designated Offices do not issue reminders to applicants in connection with the entry into the national

For detailed information about the procedural acts to be performed to enter the national phase before each designated Office, the applicable time limits and possible extensions of time or grace periods, and any other requirements, see the relevant Chapters of Volume II of the PCT Applicant's Guide. Information about the requirements for filing a demand for international preliminary examination is set out in Chapter IX of Volume I of the PCT Applicant's Guide.

GR and ES became bound by PCT Chapter II on 7 September 1996 and 6 September 1997, respectively, and may, therefore, be elected in a demand or a later election filed on or after 7 September 1996 and 6 September 1997, respectively, regardless of the filing date of the international application. (See second paragraph above.)

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

CONFIRMATION OF PRECAUTIONARY DESIGNATIONS

This notification lists only specific designations made under Rule 4.9(a) in the request. It is important to check that these designations are correct. Errors in designations can be corrected where precautionary designations have been made under Rule 4.9(b). The applicant is hereby reminded that any precautionary designations may be confirmed according to Rule 4.9(c) before the expiration of 15 months from the priority date. If it is not confirmed, it will automatically be regarded as withdrawn by the applicant. There will be no reminder and no invitation. Confirmation of a designation consists of the filing of a notice specifying the designated State concerned (with an indication of the kind of protection or treatment desired) and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.

REQUIREMENTS REGARDING PRIORITY DOCUMENTS

For applicants who have not yet complied with the requirements regarding priority documents, the following is recalled.

Where the priority of an earlier national, regional or international application is claimed, the applicant must submit a copy of the said earlier application, certified by the authority with which it was filed ("the priority document") to the receiving Office (which will transmit it to the International Bureau) or directly to the International Bureau, before the expiration of 16 months from the priority date, provided that any such priority document may still be submitted to the International Bureau before that date of international publication of the international application, in which case that document will be considered to have been received by the International Bureau on the last day of the 16-month time limit (Rule 17.1(a)).

Where the priority document is issued by the receiving Office, the applicant may, instead of submitting the priority document, request the receiving Office to prepare and transmit the priority document to the International Bureau. Such request must be made before the expiration of the 16-month time limit and may be subjected by the receiving Office to the payment of a fee (Rule 17.1(b)).

If the priority document concerned is not submitted to the International Bureau or if the request to the receiving Office to prepare and transmit the priority document has not been made (and the corresponding fee, if any, paid) within the applicable time limit indicated under the preceding paragraphs, any designated State may disregard the priority claim, provided that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity to furnish the priority document within a time limit which is reasonable under the circumstances.

Where several priorities are claimed, the priority date to be considered for the purposes of computing the 16-month time limit is the filing date of the earliest application whose priority is claimed.

1

ternational application No.

PCT/JP00/05523

CLASSIFICATION OF SUBJECT MATTER C07D491/048, A61K31/407, 31/454, 31/55, A61P9/10, 25/28, 25/16, 13/02, 9/08 According to International Patent Classification (IPC) or to both national classification and IPC FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) CO7D491/048, A61K31/407, 31/454, 31/55, Int.Cl A61P9/10, 25/28, 25/16, 13/02, 9/08 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) REGISTRY (STN), CAPLUS (STN), CAOLD (STN) C. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. Category* WO, 97/07120, Al (Smithkline Beecham P.L.C.), 1-24,29-32 27 February, 1997 (27.02.97), Claims; page 23, Example 5 & JP, 11-511156, A & EP, 1019412, A1 & US, 5972935, A 1-24,29-32 WO, 95/29177, A1 (Smithkline Beecham P.L.C.), A 02 November, 1995 (02.11.95), Claims; page 21, Example 2 & JP, 9-512025, A & EP, 757687, A1 1-24,29-32 JP, 5-339271, A (KOWA COMPANY, LTD), Α 21 December, 1993 (21.12.93), pp.3-4, Method 1 (Family: none) 'The al., 1-24,29-32 Claude, et synthesis Α Dufresne, phenylhydrazines from bis (2,2,2-trichloroethyl) azodicarboxylates and electron-rich arenes' Synth. Commun. (1997), Vol.27, No.20, p.3613-3624, Compound No. 22 See patent family annex. Further documents are listed in the continuation of Box C. later document published after the international filing date or Special categories of cited documents: document defining the general state of the art which is not priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention considered to be of particular relevance earlier document but published on or after the international filing document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive document which may throw doubts on priority claim(s) or which is step when the document is taken alone cited to establish the publication date of another citation or other document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is special reason (as specified) combined with one or more other such documents, such document referring to an oral disclosure, use, exhibition or other combination being obvious to a person skilled in the art document member of the same patent family document published prior to the international filing date but later than the priority date claimed Date of mailing of the international search report Date of the actual completion of the international search 05 December, 2000 (05.12.00) 22 November, 2000 (22.11.00) Authorized officer Name and mailing address of the ISA/ Japanese Patent Office Telephone No. Facsimile No.

PCT/JP00/05523

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet) This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons: Claims Nos.: 25-28 because they relate to subject matter not required to be searched by this Authority, namely: Claims 25 to 28 pertain to methods for treatment of the human body by therapy, and thus relate to subject matters which this International Searching Authority is not required, under the provisions of Article 17(2)(a)(i) of the PCT and Rule 39.1(iv) of the Regulations under the PCT, to search. Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically: Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a). Observations where unity of invention is lacking (Continuation of item 2 of first sheet) This International Searching Authority found multiple inventions in this international application, as follows: As all required additional search fees were timely paid by the applicant, this international search report covers all searchable As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.: No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: The additional search fees were accompanied by the applicant's protest. Remark on Protest No protest accompanied the payment of additional search fees.



出願人又は代理人

の告類記号 2628WO0P

特 許 協 力 条 約

今後の手続きについては、国際予備審査報告の送付通知(様式PCT/

特許庁審査官(権限のある職員

電話番号 03-3581-1101 内線

新留 豊

IPEA/416)を参照すること。

PCT

国際予備審査報告

(法第12条、法施行規則第56条) [PCT36条及びPCT規則70]



9639

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国際出願番号 PCT/JP00/05523	(4.71. 4)	8. 08. 00	優先日 (日.月.年)	20.08.99
国際特許分類 (IPC) Int. Cl ⁷ 31/55, A61P9/10, 25/2			/407, 31,	/454,
出願人(氏名又は名称) 正代 日	薬品工業 核	朱式会社		
1. 国際予備審査機関が作成したこの目	国際予備審査報告を注	去施行規則第57条(P(こT36条)の規	定に従い送付する。
2. この国際予備審査報告は、この表紙	紙を含めて全部で _	5 ペーシ	ごからなる。	
この国際予備審査報告には、附属書類、つまり補正されて、この報告の基礎とされた及び/又はこの国際予備 査機関に対してした訂正を含む明細書、請求の範囲及び/又は図面も添付されている。 (PCT規則70.16及びPCT実施細則第607号参照) この附属書類は、全部で ページである。				/又はこの国際予備審
3. この国際予備審査報告は、次の内容				
I V 国際予備審査報告の基礎				
Ⅱ □ 優先権				
Ⅲ ☑ 新規性、進歩性又は産業	上の利用可能性につ	いての国際予備審査報	告の不作成	
IV 発明の単一性の欠如				
V V PCT35条(2)に規定す	よい ような とうだい ような とうしゅう とうしゅう かいま とうしゅう かいま かいま かいま かいま かいま しゅう かいま しゅう	又は産業上の利用可能性	tについての見解	、それを裏付けるため
の文献及び説明 VI ある種の引用文献				
VII 国際出願の不備				
Vm V 国際出願に対する意見	VIII VIII 国際出願に対する意見			
		T		
国際予備審査の請求書を受理した日	•	国際予備審査報告を代	F成した日 7 03 01	

東京都千代田区霞が関三丁目4番3号

日本国特許庁 (IPEA/JP) 郵便番号100-8915

名称及びあて先



国際予備審査報告

国際出願番号 PCT/JP00/05523

I.		国際予備審查報	告の基礎		
1.	この国際予備審査報告は下記の出願書類に基づいて作成された。(法第6条(PCT14条)の規定に基づく命令に 応答するために提出された差し替え用紙は、この報告書において「出願時」とし、本報告書には添付しない。 PCT規則70.16,70.17)				
	V	出願時の国際	出願書類		
		明細書 明細書 明細書	第 ページ、 出願時に提出されたもの 第 ページ、 国際予備審査の請求書と共に提出されたもの 第 ページ、 付の書簡と共に提出されたもの		
		請求の範囲 請求の範囲 請求の範囲 請求の範囲	第 項、 出願時に提出されたもの 第 項、 PCT19条の規定に基づき補正されたもの 第 項、 国際予備審査の請求書と共に提出されたもの 第 項、 付の書簡と共に提出されたもの		
		図面 図面 図面	第ページ/図、 出願時に提出されたもの 第ページ/図、 国際予備審査の請求書と共に提出されたもの 第 付の書簡と共に提出されたもの		
		明細書の配列	表の部分 第ページ、出願時に提出されたもの表の部分 第ページ、国際予備審査の請求書と共に提出されたもの表の部分 第ページ、付の書簡と共に提出されたもの		
3.	 2. 上記の出願書類の言語は、下記に示す場合を除くほか、この国際出願の言語である。 上記の書類は、下記の言語である 語である。 国際調査のために提出されたPCT規則23.1(b)にいう翻訳文の言語 PCT規則48.3(b)にいう国際公開の言語 国際予備審査のために提出されたPCT規則55.2または55.3にいう翻訳文の言語 3. この国際出願は、ヌクレオチド又はアミノ酸配列を含んでおり、次の配列表に基づき国際予備審査報告を行った。 				
	1	この国際に 出願後に 出願後に 出願後に 書の提出	5配列表に記載した配列とフレキシブルディスクによる配列表に記録した配列が同一である旨の陳述		
4.		明細書	記の書類が削除された。 第ページ 第項 図面の第 ページ/図		
5.	5. □ この国際予備審査報告は、補充欄に示したように、補正が出願時における開示の範囲を越えてされたものと認められるので、その補正がされなかったものとして作成した。(PCT規則70.2(c) この補正を含む差し替え用紙は上記1. における判断の際に考慮しなければならず、本報告に添付する。)				



国際予備審査報告

国際出願番号 PCT/JP00/05523

П.	新規性、進歩性又は産業上の利用可能性についての国際予備審査報告の不作成
1.	次に関して、当該請求の範囲に記載されている発明の新規性、進歩性又は産業上の利用可能性につき、次の理由により 審査しない。
	国際出願全体
Ī	請求の範囲 25-28
_	
理由	:
	この国際出願又は請求の範囲 25-28 は、国際予備審査をすることを要しない 大の事項を内容としている(具体的に記載すること)。 請求の範囲 25-28は、治療による人体の処置方法に関するものであって、 PCT34条(4)(a)(i)及びPCT規則67.1(i v)の規定により、この国際予備審査機関が国際予備審査を行うことを要しない対象に係るものである。
	月細書、請求の範囲若しくは図面(次に示す部分)又は請求の範囲の記載が、不明確であるため、見解を示すことができない(具体的に記載すること)。
	全部の請求の範囲又は請求の範囲が、明細 書による十分な 篡付けを欠くため、見解を示すことができない。
V	†求の範囲 <u>25-28</u> について、国際調査報告が作成されていない。
2.	ヌクレオチド又はアミノ酸の配列表が実施細則の附属曹C(塩基配列又はアミノ酸配列を含む明細曹等の作成のための ガイドライン)に定める基準を満たしていないので、有効な国際予備審査をすることができない。
•	書面による配列表が提出されていない又は所定の基準を満たしていない。
	 フレキシブルディスクによる配列表が提出されていない又は所定の基準を満たしていない。



国際予備審査報告

国際出願番号 PCT/JP00/05523

v.	新規性、進歩性又は産業上の利用可能 文献及び説明	生についての法第12条(P 	CT35条(2)) に定める見解、	それを裏付ける
1.	見解			
	新規性(N)	請求の範囲 請求の範囲	1-24, 29-32	有

1-24, 29-32 有

産業上の利用可能性 (IA)

請求の範囲 <u>1-24,29-32</u> 有 請求の範囲 無

2. 文献及び説明 (PCT規則70.7)

文献 1: WO, 97/07120, A1 (Smithkline Beecham P. L. C.), 27.2月.97 (27.02.97)

文献 2: WO, 95/29177, A1 (Smithkline Beecham P. L. C.), 2.11月.95 (02.11.95)

文献 3: JP, 5-339271, A (興和株式会社), 21.12月.1993 (21.12.93)

文献 4: Dufresne, Claude, et al., 'The synthesis of phenylhydrazines from

bis (2, 2, 2-trichloroethyl) azodicarboxylates and electron-rich arenes' Synth. Commun. (1997), Vol. 27, No. 20, p. 3613-3624

説明:

文献1-4には、本願化合物と類似構造のフロインドール化合物、あるいはフロキ ノリン化合物が記載されている。

特許文献である文献1-3には、本願請求の範囲の化合物も含みうる包括的な構造式が記載されているが、本願請求の範囲に含まれうる化合物は実際に製造されてはいない。

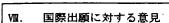
そして、文献1-4に記載の化合物はそれぞれセロトニン拮抗剤、抗不整脈あるいは他の化合物の原料として記載されているのみであり、本願の化合物が有する作用は記載されていない。

したがって、過酸化脂質生成抑制作用を有する本願の化合物を製造、使用することは、文献1-4の記載から当業者に自明でない。

よって、請求の範囲1-24,29-32に係る発明は、進歩性を有する。

請求の範囲1-24、29-32に係る発明は、産業上の利用可能性を有する。





請求の範囲、明細書及び図面の明瞭性又は請求の範囲の明細書による十分な裏付についての意見を次に示す。

請求の範囲は、開示された実施例を合理的に一般化したもので、かつ該範囲に包含される化合物がすべて、発明の課題を実際に解決するものであるように記載されるべきである。本願の場合、実際に製造され試験された化合物が、比較的限定されたものである事を考慮すると、請求の範囲1-13, 18-25, 30-33が合理的で正当であると判断しうるかは疑問である。

上記請求の範囲に記載の「含窒素複素環基」、「芳香族複素環基」、「炭化水素基」、「プロドラッグ」等の表現、あるいは特定の置換基を明示せず、ただ「さらに置換されてもよい」とする表現は、当該表現が指摘ないし暗示する原子団において、どのような原子がどのような相互関係にあるのか、具体的に示されていない。これらについては明細書中で若干の例示があるのみで、さらに具体的に定義されることなく使用されているため、不明確かつ不確定的であり、出願人が主張する効果を奏さない想像上の化合物を想起させるものである。

加えて、上記例示を考慮して具体的な化合物が把握できたとしても、実際に製造・ 使用された化合物の範囲が狭いため、これらと同様の効果が全体にわたり十分推定さ れるとは認められない。

上記請求の範囲はこれらの化合物を包含するため、該請求の範囲全体について十分な裏付けがあるとは認められない。

2. 請求の範囲21-24,30-32に記載の各疾患について、本願化合物がこれらの治療に直接有用であることが漠然と記載されているのみで、データに基づく裏付けはない。そして、実際に確認されている過酸化脂質生成抑制作用と、これらの疾患との関連も直接的な因果関係を有するものとしては説明されていない。したがって、上記請求の範囲に係る発明は十分に裏付けられていない。

Translation



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 2628WO0P	FOR FURTHER ACTION	SeeNotificationofTransmittalofInternational Preliminary Examination Report (Form PCT/IPEA/416)		
International application No. PCT/JP00/05523				
International Patent Classification (IPC) or n C07D 491/048, A61K 31/407, 3		/28, 25/16, 1	3/02, 9/08	
Applicant	KEDA CHEMICAL INDU	JSTRIES, L	.TD.	
This international preliminary exami and is transmitted to the applicant ac		by this Intern	national Preliminary Examining Authority	
2. This REPORT consists of a total of	5 sheets, including	ng this cover s	heet.	
This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (Rule 70.16 and Section 607 of the Administrative Instructions under the PCT). These annexes consist of a total of sheets.				
3. This report contains indications rela	ting to the following items:			
Basis of the report				
II Priority				
III Non-establishment o	of opinion with regard to novelt	y, inventive st	ep and industrial applicability	
IV Lack of unity of inve	· ·	,		
Reasoned statement		l to novelty, in it	ventive step or industrial applicability;	
VI Certain documents of	cited			
VII Certain defects in th	e international application			
VIII Certain observations	s on the international applicatio	n .		
Date of submission of the demand	Date o	f completion of	of this report	
29 September 2000 (29.	.09.00)	27 1	March 2001 (27.03.2001)	
Name and mailing address of the IPEA/JP	Autho	rized officer		
Facsimile No.	Telepi	Telephone No.		

I. Basis	of the report	
I. With	regard to the elements of the international application:*	
\boxtimes	the international application as originally filed	
	the description:	
_	pages	, as originally filed
	pages	filed with the demand
	pages	, filed with the letter of
	the claims:	
	pages	. as originally filed
	pages	, as amended (together with any statement under Article 19
		, filed with the demand
	pages	_, filed with the letter of
	the drawings:	
	pages	, as originally filed
	pages	. filed with the demand
	pages	, filed with the letter of
	the sequence listing part of the description:	
	pages	, as originally filed
	pages	, filed with the demand
	pages	, filed with the letter of
	the language of a translation furnished for the purposes of it the language of publication of the international application	
3. With preli		e disclosed in the international application, the international ice listing:
	contained in the international application in written form.	
	filed together with the international application in computer	readable form.
	furnished subsequently to this Authority in written form.	
	furnished subsequently to this Authority in computer readab	ole form.
. \square	The statement that the subsequently furnished written international application as filed has been furnished.	sequence listing does not go beyond the disclosure in the
	The statement that the information recorded in computer been furnished.	readable form is identical to the written sequence listing has
4.	The amendments have resulted in the cancellation of:	
	the description, pages	
	the claims, Nos.	
	the drawings, sheets/fig	·
5.	This report has been established as if (some of) the amenda beyond the disclosure as filed, as indicated in the Supplement	nents had not been made, since they have been considered to go
in th	acement sheets which have been furnished to the receiving O is report as "originally filed" and are not annexed to the	Tice in response to an invitation under Article 14 are referred to its report since they do not contain amendments (Rule 70.16
ana i	<i>(0.17)</i> .	·
KIIY I	replacement sheet containing such amendments must be refer	rea to under item 1 and annexed to this report.

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III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:
the entire international application.
Claims Nos
because:
the said international application, or the said claims Nos. 25-28 relate to the following subject matter which does not require an international preliminary examination (specify):
The subject matter of Claims 25-28 relates to a method for treatment of the human body by therapy, which does not require an international preliminary examination by the International Preliminary Examining Authority in accordance with PCT Article 34(4)(a)(i) and Rule 67.1(iv).
the description, claims or drawings (indicate particular elements below) or said claims Nosare so unclear that no meaningful opinion could be formed (specify):
the claims, or said claims Nos are so inadequately supported by the description that no meaningful opinion could be formed.
no international search report has been established for said claims Nos
2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid
sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions: the written form has not been furnished or does not comply with the standard.
the computer readable form has not been furnished or does not comply with the standard.
List in the standard.

INTERNATIONAL PI

MINARY EXAMINATION REPORT

٧.	Reasoned statement under Article 35(2) with rega	rd to novelty, inventive step or	industrial applicability;
	citations and explanations supporting such staten	nent	

tatement			
Novelty (N)	Claims	1-24,29-32	YE
	Claims		 NC
Inventive step (IS)	Claims	1-24,29-32	 YE
	Claims		 NC
Industrial applicability (IA)	Claims	1-24,29-32	_ YE
	Claims		NO

2. Citations and explanations

Document 1: WO, 97/07120, A1 (Smithkline Beecham P. L. C.) 27 February 1997 (27.02.97)

Document 2: WO, 95/29177, A1 (Smithkline Beecham P. L. C.) 2 November 1995 (02.11.95)

Document 3: JP, 5-339271, A (Kowa Co., Ltd.) 21 December 1993 (21.12.93)

Document 4: Dufresne, Claude, et al., "The synthesis of phenylhydrazines from bis(2,2,2-trichloroethyl) azodicarboxylates and electron-rich arenes," Synth. Commun., Vol. 27, No. 20, 1997, pp. 3613-3624

Documents 1-4 describe furo-indole compounds or furo-quinoline compounds with structures similar to the compounds of this application.

Documents 1-3, which are patents, describe broad structural formulas that may include the compounds of the Claims of this application, but the compounds that may be included in the Claims of this application were not actually produced.

Furthermore, the compounds set forth in documents 1-4 are only described as starting materials for serotonin antagonists, anti-arrhythmic agents and other compounds, and the effects of the compounds of this application are not described.

Therefore, the production and use of the inventive compounds having inhibitory action against the formation of lipoperoxide is not self-evident to persons skilled in the art based on the descriptions in documents 1-4.

As a result, the inventions set forth in Claims 1-24 and 29-39 appear to involve an inventive step.

The inventions set forth in Claims 1-24 and 29-32 also appear to have industrial applicability.

PCT/JP00/05523

VIII. Certain observations on the international application

The following observations on the claims are fully supported by the description, are made:

The Claims are a logical generalization of the Examples that are disclosed, and all compounds included within the scope of the Claims should be described such that they actually solve the inventive problem. In the case of this application, in light of the fact that the number of compounds actually produced and tested was relatively limited, it is impossible to decide if the scope of Claims 1-13, 18-25, and 30-33 is logically valid.

The expressions "heterocyclic group containing nitrogen," "aromatic heterocyclic group," hydrocarbon group," "prodrug," and the like and expressions in which specific substituents are not delineated and the term "optionally substituted" is used do not specifically express what kinds of relationships exist between what kinds of atoms in the groups of atoms that these expressions refer to or imply. The Specification contains only a small number of Examples, and because these expressions are used without specific definitions, they are vague and imprecise, and it is possible to imagine compounds that do not bring about the effect asserted by the applicant.

Furthermore, even if it were possible to figure out specific compounds from the above Examples, because the scope of compounds that were actually produced and used is narrow, this examination finds that it is impossible to assume that all of the compounds will have effects similar to those in the Examples.

Therefore, this examination finds that because the Claims include these compounds, all the compounds of the Claims are insufficiently supported by the Specification.

2. With respect to the various diseases listed in Claims 21-24 and 30-32, there is only a vague statement that the inventive compounds are directly useful in the treatment of these diseases, and there is no data to support these assertions. In addition, the link between the action of inhibiting the formation of lipoperoxide, which has actually been verified, and these diseases is not explained as one having a direct cause-effect relationship.

Therefore, the inventions set forth in the above Claims are not sufficiently supported.

(19) 世界知的所有権機関 国際事務局



(43) 国際公開日 2001 年3 月1 日 (01.03.2001)

PCT

(10) 国際公開番号 WO 01/14384 A1

(51) 国際特許分類7: C07D 491/048, A61K 31/407, 31/454, 31/55, A61P 9/10, 25/28, 25/16, 13/02, 9/08

(21) 国際出願番号:

PCT/JP00/05523

(22) 国際出願日:

2000年8月18日(18.08.2000)

(25) 国際出願の言語:

日本語

(26) 国際公開の言語:

日本語

(30) 優先権データ:

特願平11/234718 1999年8月20日(20.08.1999) JP

(71) 出願人 (米国を除く全ての指定国について): 武田薬品 工業株式会社 (TAKEDA CHEMICAL INDUSTRIES, LTD.) [JP/JP]; 〒541-0045 大阪府大阪市中央区道修町 四丁目1番1号 Osaka (JP). (72) 発明者; および

(75) 発明者/出願人 (米国についてのみ): 大川滋紀 (OHKAWA, Shigenori) [JP/JP]; 〒 569-1121 大阪府高槻市真上町6丁目45番20号 Osaka (JP). 橋本忠俊 (HASHIMOTO, Tadatoshi) [JP/JP]; 〒 567-0828 大阪府茨木市舟木町6番26-1301 Osaka (JP). 塚本徹哉 (TSUKAMOTO, Tetsuya) [JP/JP]; 〒 674-0084 兵庫県明石市魚住町西岡2376番地の7 Hyogo (JP).

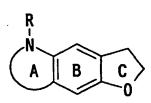
(74) 代理人: 弁理士 高橋秀一, 外(TAKAHASHI, Shuichi et al.); 〒532-0024 大阪府大阪市淀川区十三本町2丁 目17番85号 武田薬品工業株式会社 大阪工場内 Osaka (JP).

(81) 指定国 (国内): AE, AG, AL, AM, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PL, RO,

[続葉有]

(54) Title: TRICYCLIC DIHYDROBENZOFURAN DERIVATIVES, PROCESS FOR THE PREPARATION THEREOF AND AGENTS

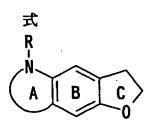
(54) 発明の名称: 三環性ジヒドロベンゾフラン誘導体、その製造法及び剤



(1)

(57) Abstract: Compounds represented by general formula (1) or salts thereof exhibit excellent inhibitory activity against the formation of peroxylipid and are useful as inhibitors against the formation thereof. In said formula, A is a nonaromatic five-to seven-membered nitrogenous heterocycle which may be additionally substituted; B is a benzene ring which is additionally substituted; C is a dihydrofuran ring which may be additionally substituted; and R is hydrogen or acyl.

(57) 要約:



〔式中、A環は更に置換基を有していてもよい非芳香族5ないし7員含窒素複素環を、B環は更に置換基を有するペンゼン環を、C環は更に置換基を有していてもよいジヒドロフラン環を、Rは水素原子又はアシル基を示す。〕で表される化合物又はその塩は、優れた過酸化脂質生成抑制作用を有し、過酸化脂質生成抑制剤として有用である。

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RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA.

(84) 指定国 (広域): ARIPO 特許 (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), ユーラシア特許 (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), ヨーロッパ特許 (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI 特許 (BF, BJ, CF, CG, CI,

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